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Incidence of cardiovascular complications in knee arthroplasty patients before and after implementation of a ropivacaine local infiltration analgesia protocol: A retrospective study

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ABSTRACT

Background: Local infiltration analgesia (LIA) during total knee arthroplasty has been shown to give statistically significant reduction in post-operative pain. The effects of using high volumes of ropivacaine combined with adrenaline as LIA on cardiovascular parameters in knee replacement have not been described before. The objective of this study was to investigate the cardiovascular safety of ropivacaine as part of high volume local infiltration analgesia (LIA) in total knee replacement surgery.
Methods: This is a retrospective observational comparative cohort study conducted in two independent cohorts, one treated without and one treated with a local infiltration analgesia protocol, containing a total of 744 patients with a mean age of 68 years (42 to 89) and 68 years (21 to 88) respectively with a follow-up of 12 months.
Results: No statistical difference in bradycardia during surgery, post-operative cardiovascular complications, and mortality was found after use of LIA. A statistically significant lower incidence of hypotension was found in the LIA group ($P < 0.01$). This result has to be interpreted with care, due to the use of adrenaline in the LIA mixture, which could mask possible hypotension. No statistical difference was found in the occurrence of hypertension or tachycardia, despite the addition of adrenaline to the LIA mixture. No difference in mortality was found between the two groups ($P = 0.11$).
Conclusion: These results show safe use of high volume ropivacaine with adrenaline as local infiltration analgesia during total knee replacement surgery.

1. Introduction

Post-operative pain and adverse effects related to medication can impair early post-operative mobilization after total knee arthroplasty and may cause a prolonged length of hospital stay. Several studies have been performed to assess peri-operative, multimodal protocols for post-operative pain reduction and early mobilization [1–6]. The main focus of these fast-track protocols is to reduce post-operative pain and reduce the need for opioid medication, which leads to faster mobilization after surgery. These fast track protocols are becoming increasingly popular in total knee arthroplasty and total hip arthroplasty as opposed to protocols with epidural analgesia or peripheral nerve blocks, which can have side effects that impair early mobilization [1–11].

Local infiltration analgesia (LIA) during total knee arthroplasty as part of fast-track protocols has been shown to give a reduction in post-operative pain and opioid medication consumption. In LIA infiltration, high volumes of 150 cm^3 up to 300 cm^3 of 0.2% ropivacaine are applied behind the posterior capsule of the knee, in the gutters, in the peripatellar and periosteal space and in the subcutaneous tissue during surgery. This is necessary to cover the areas where surgical intervention has taken place to achieve an optimal result in reducing post-operative pain [12–15].

Cardiac and central nervous system toxicity can be complications of longer acting local anesthetics such as bupivacaine or ropivacaine, with better cardiovascular safety reported for ropivacaine [16–20]. Pre-operative cardiovascular effects of ropivacaine specifically after high volume LIA infiltration during total knee replacement have not been reported in detail before. Our hypothesis is that there is no difference in the incidence of bradycardia and hypotension during surgery and no difference in post-operative cardiovascular complications between patients treated before and after implementation of a LIA protocol for the reduction of post-operative pain.

2. Materials and methods

2.1. Outcome measures

Primary outcomes were defined as the incidence of hypotension and bradycardia during surgery, and the post-operative incidence of cardiac

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arrhythmias and myocardial infarction. As secondary outcome measure mortality was monitored during the first 12 months after surgery.

2.2. Informed consent and selection of participants

This study met the criteria for exemption for obtaining informed consent. The study was conducted with one independent cohort receiving the standard treatment protocol in knee arthroplasty (cohort 1) and one independent cohort (cohort 2) also receiving the LIA protocol, the protocols are summarized in Appendices A and B respectively. The patients in cohort 1 were enrolled between November 2011 and November 2012 at the Rijnland Hospital Leiderdorp (performing ~400 knee arthroplasties annually). Patients for cohort 2 were enrolled between November 2012 and November 2013.

From November 2011 until November 2012 all patients with knee arthroplasties were screened for eligibility and included in cohort 1. Patients admitted for revision of their total knee prosthesis, patients receiving hemi prostheses, patients receiving tumor prosthesis or rotating hinge prosthesis, patients scheduled for patellofemoral resurfacing and patients with missing surgery records were excluded. In November 2012 a LIA protocol was introduced in the orthopedic department at the Rijnland Ziekenhuis with the main purpose of reducing post-operative pain, improving early mobilization and thereby reducing length of stay. During the period of November 2012 up to November 2013 patients treated with the LIA protocol were included in cohort 2. Patients treated according to the previous protocol or receiving epidural anesthesia were excluded from analysis. For this cohort, the same exclusion criteria from cohort 1 were used, with the addition of the exclusion of patients not treated according to the LIA protocol.

2.3. LIA

In the LIA protocol during surgery, infiltration of 50 cm^3 of 0.2% ropivacaine with one milligram of adrenalin in the posterior joint capsule, 50 cm^3 of 0.2% ropivacaine with one milligram of adrenaline in the peripatellar and periosteal space and gutters and 50 cm^3 of ropivacaine 0.2% without adrenaline in the subcutaneous tissue was used. No drain was inserted during surgery to allow for early mobilization. In both procedures, patients were treated with compression bandages afterwards for 24 h.

2.4. Data collection

All the variables mentioned in the tables were retrospectively registered in the digital hospital information system Xcare Patient (McKesson, San Fransisco, USA). Data was extracted from discharge letters, anesthesiology reports, surgery reports and the patients' clinical file (both written and electronic versions). The files used for obtaining data are specified in Appendix D.

In the patients treated with the standard peri-operative protocol, bradycardia during surgery was described as either present or not present and was defined as a heart rate lower than 60 beats per minute during three consecutive measurements during surgery. Hypotension during surgery was described as either present or not present and was defined as a systolic pressure lower than 90 mm Hg or a diastolic pressure lower than 60 mm Hg during two consecutive measurements during surgery.

In cohort 2, treated with the LIA protocol, bradycardia was described in three different ways: first whether bradycardia was seen throughout the entire surgery, second whether bradycardia was already present before LIA was administered and no sudden increase of bradycardia was monitored after administration of LIA and thirdly, whether bradycardia was monitored for the first time after administration of LIA, and whether there was a direct relation between onset of bradycardia and moment of LIA administration. Hypotension during surgery in cohort 2 was described in the same way as was bradycardia in cohort 2. The specific definition used for bradycardia and hypotension in both cohorts can be found in Appendix D.

Patients were followed until 12 months post-operatively and complications were registered from discharge letters, surgery reports, electronic files and complication registration databases. This follow-up duration was chosen because 12-month follow-up data was available through the database, which was also built for other research purposes.

2.5. Data analysis

Data were presented as mean (standard deviation: SD) if normally distributed and median. (Interquartile range: IQR) if data were rightly skewed. Distribution of data was analyzed with the Shapiro–Wilk test. Descriptive categorical data were analyzed using X^2-tests. Continuous data were analyzed with a Student's *t*-test when appropriate.

Binary logistic regression was used to analyze confounding effect of pre-operative hemoglobin levels, American Society of Anaesthesiologists-scores, type of anesthesia on bradycardia and hypotension. Correction was performed for multiple measurements. Stratification of cohorts was used to correct for potential confounders.

Binary logistic regression was used to analyze the association between LIA administration and the incidence of atrial fibrillation, other cardiac arrhythmias and myocardial infarction. Each complication was analyzed separately and correction for multiple measurements was performed. No stepwise regression was used in the statistical analysis. P-value of $P < 0.05$ was considered statistically significant. All data were analyzed using SPSS statistics (SPSS version 21.0, IBM, New York, USA).

3. Results

3.1. Patient characteristics and inclusion

Initially, 849 knee arthroplasty patients were screened for eligibility. For cohort 1, treated according to the standard knee protocol, 417 patients were screened for eligibility. After screening, 38 patients were excluded from analysis, leaving 379 primary total knee patients eligible for inclusion in this study. Patients were excluded because they needed revision surgery (N = 22), patella resurfacing (N = 12), hemi prosthesis/tumor prosthesis (N = 3) or data were missing (N = 1). In cohort 2, 432 knee arthroplasty patients were screened for eligibility. After screening, 68 patients were excluded from analysis, leaving 365 primary knee arthroplasty patients eligible for inclusion in this study. Patients were excluded because they needed revision surgery (N = 40), patellar resurfacing (N = 12), hemi prosthesis/tumor prosthesis (N = 3) or did not receive local anesthetic infiltration (N = 3). Data were missing in 10 patients, which after research appeared to be lost in the process of digitalizing patient files. This was also true for the patient in cohort 1 with missing data. In Appendix C the number per exclusion criterion is reported.

In Table 1, patient characteristics for each cohort are presented. The two cohorts were comparable at baseline, except for ASA scores and cardiac arrhythmias (other than atrial fibrillation) e.g. supraventricular extrasystoles. (See Table 1.)

3.2. Bradycardia during surgery

In the patients treated by the LIA protocol 96 people presented with bradycardia during surgery versus 107 people in the group treated without ropivacaine. Bradycardia occurring for the first time during surgery after administration of ropivacaine was seen in seven patients. The mean time that elapsed after LIA administration was 12 min, ranging from five to 30 min. In the other 89 patients bradycardia had already been present before infiltration and no new episode of bradycardia occurred after infiltration. The difference in number of patients presenting with bradycardia before and after implementation of the LIA protocol was not statistically significant (Pearson's X^2-test P 0.55).

3.3. Hypotension during surgery

Hypotension during surgery occurred in 250 patients treated with the standard knee prosthesis protocol. In the LIA protocol, 205 patients had an episode of hypotension during surgery. The first episode of hypotension occurred after LIA infiltration in 18 patients. The mean time elapsed after infiltration was 16 min, ranging from five to 35 min. In the other 187 patients, hypotension was not directly related to LIA administration. The difference in hypotension was analyzed and proved to be statistically significant (Pearson's X^2-test $P < 0.01$).